UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/517,880	12/13/2004	Shuo Lin	30435145USWO	4614

22462 7590 04/25/2007

GATES & COOPER LLP
HOWARD HUGHES CENTER
6701 CENTER DRIVE WEST, SUITE 1050
LOS ANGELES, CA 90045

EXAMINER	
BERTOGLIO, VALARIE E	
ART UNIT	**PAPER NUMBER**
1632	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/25/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/517,880	LIN, SHUO	
	Examiner	Art Unit	
	Valarie Bertoglio	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 March 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4,5,7-9,11-18,20,22 and 23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4,5,7-9,11-18,20,22-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *13 December 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's request for reconsideration of the finality of the rejection of the last Office action is persuasive and, therefore, the finality of that action is withdrawn.

Applicant's reply dated 03/26/2007 has been entered. Claims 5,11,and 23 have been amended. Claims 3,6,10,19 and 21 are cancelled. Claims 1,2,4,5,7-9,11-18,20,22-23 are under consideration in the instant office action.

Claim Objections

Claims 11,22 and 23 are objected to because of the following informalities: The preamble of the claim is limited to an oviparous fish. However, the method steps in the body of the claim are not so limited. Appropriate correction is required.

Claim Rejections - 35 USC § 112-1st paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The previous rejection of claims 5,11-18 and 20,22 and 23 under 35 U.S.C. 112, first paragraph, because the specification, is not enabling for the full breadth of the claim is withdrawn.

Claims 11,22 and 23 are directed to an oviparous teleost fish, however, the claim is objected to as set forth above. Failure to amend the body of the claims accordingly along with removal of the term "oviparous" from the preamble would necessitate reinstatement of this presently withdrawn grounds of rejection.

Claim 5 has been amended to be limited to same-species nuclear transfer and thus is now enabled as it fails to encompass making fertile offspring by way of cross-species nuclear transfer. Claim 11 no longer requiresthat the offspring be fertile. Thus the rejection on this grounds is withdrawn as well.

A new grounds of rejection is set forth below. As a result, the instant action is non-final.

Claims 1,2,4,5,7-9,11-18,20,22-23 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for 1) a method of making a diploid transgenic teleost fish comprising introducing an exogenous nucleic acid into the genome of a cultured embryonic fibroblast derived from a progenitor *Danio rerio* (zebrafish) embryo, transplanting the nucleus of the resulting transformed cell into an enucleated egg from a parental fish, wherein the parental fish is of the same species as the progenitor if fertile progeny are desired (claim 5), culturing the resultant embryo in conditions suitable for embryonic development such that a diploid transgenic fish is made and for 2) a method of making an oviparous teleost fish comprising obtaining a cell from a progenitor *Danio rerio* (zebrafish) embryo, maintaining the cell in in vitro culture, transplanting the nucleus of the cultured cell into an enucleated egg from a parental fish of the same species as the progenitor and culturing the resultant embryo in conditions suitable for embryonic development such that a fertile progeny fish is made a does not reasonably provide enablement for use of a donor cell, as claimed, from any species other than Danio rerio. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Enablement is considered in view of the Wands factors (MPEP 2164.01(a)). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (*Wands*, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the

invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (*Wands*, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

The claims encompass use of a donor embryonic cell from any oviparous fish species. The specification teaches use of a cultured cell from a zebrafish embryo. However, the state of the art at the time of filing showed that maintaining a cell in culture for nuclear transfer was not routine for any species of fish. Murphey and Zon (2002, **Nature Biotechnology**, 20:785-786) state that nuclear transfer studies in fish have been ongoing since the 1960s, however, fertile diploid adults had never been consistently generated. Liu *et al.* (2002, IDS) reported that with each passage of cells from embryos the developmental rate of nuclear transfer embryos made from the nuclei of the cells decreased. Liu *et al.* hypothesize that with successive passages, genetic damage accumulates (page 723, col. 1, paragraph 2). Lee *et al.* note that all previous experiments involving fish donor cells have been noncultured blastula cells, which have limited potential for genetic manipulation (August 2002, IDS). Chen *et al* (2002, **Aquaculture**, 214:67-79) note many successes in nuclear transplantation in multiple species, using blastula nuclei. However, only a single medaka ES-like cell line was shown to retain an eudiploid karyotype and the ability to form viable chimeras (paragraph bridging pages 68-69). Lee *et al* report the first successful cloning of fertile fish using long-term cultured zebrafish cells. According to Murphey and Zon, the culture conditions of Shuo Lin (the inventor of the instant invention) and colleagues at that time (August, 2002) brought about a revolutionary change in enabling the long-term culture of cells to allow for genetic alteration.

Thus, because the technology necessary to culture fish cells for nuclear transfer was highly underdeveloped at the time of filing, the specification is only enabled for use of cells from zebrafish embryos and not from other species of fish. The specification fails to provide the guidance necessary to overcome the underdeveloped state of art for use of any donor cell nucleus as claimed from any fish embryo other than Danio rerio. It would require an undue experimentation to determine how to culture cells for genetic modification and nuclear transfer in any other species. Thus, the claims should be further limited to use of zebrafish embryonic fibroblasts as nuclear donors.

Claim Rejections - 35 USC § 112-2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 5 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The phrase "resulting in the transgenic fish being fertile" is unclear as written because it is not clear whether the method as a whole results in a fertile fish or whether the phrase is a direct effect of the parental fish being of the same species. As written, the phrase is not further limiting and does not necessarily require that the resultant fish be fertile. The claim would be more clear if it read "and wherein the resulting transgenic fish is fertile".

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The rejection of claim 21 under 35 U.S.C. 102(b) as being anticipated by or, in the alternative, as obvious over Kawakami *et al.* [2000, **Current Biology**, 10:463-466] is withdrawn in light of Applicant's cancellation of the claim.

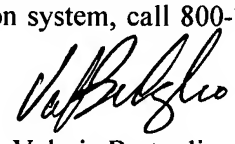
Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Valarie Bertoglio whose telephone number is (571) 272-0725. The examiner can normally be reached on Mon-Thurs 5:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on (571) 272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



Valarie Bertoglio
Primary Examiner
Art Unit 1632